REMARKS

Claims 1-26 are pending in this application. Claims 1-4, 9-18, and 23-26 have been withdrawn from consideration. Claims 5-8, and 19-22 have been rejected. None of the claims have been objected to.

In view of the following amendment and response, the Applicant believes the claims presented herein are allowable. Reconsideration is respectfully requested.

REJECTIONS UNDER 35 U.S.C. §112, SECOND PARAGRAPH

Claims 5-8, and 19-22 are rejected under 35 U.S.C. §112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. Applicant respectfully asserts that due to amendments made to the existing claims, this rejection is now traversed. Specifically, Applicant amended Claim 5 to clarify "COPD" as "Chronic Obstructive Pulmonary Disease." In addition, Applicant amended the claims to more distinctly point out "soluble E-cadherin" as "sE-cadherin."

Regarding the Examiner's objection to use of "soluble E-cadherin" in claims 5-8 and 19-22, Applicant respectfully asserts that use of "soluble E-cadherin" or "sE-cadherin" does not render the claims indefinite. Soluble E-cadherin is a term known in the prior art to be a particular form of E-cadherin. The attached British Journal of Cancer paper (*Brit. J. Cancer* (1996) 74:579-584) describes sE-cadherin as an 80kDa fragment of E-cadherin (p.579, final paragraph) and explains that this molecule can be formed by degradation of E-cadherin in-vitro (p.583, right hand column lines 8-12), but that it is not clear whether it may also have a biological role of its own right (p.583, right hand column lines 3-8). The following attached references also refer to sE-cadherin; Pasdar *et al. Cell Growth & Differentiation*, 8:4:451-462; Damsky *et al, Cell* (1983) 34:455–466, indicating that this molecule was well known and that its possible biological significance was the subject of intensive study, prior to the date of the current application. In fact the patent specification itself includes a reference to a publication, Matsuyoshi, N *et al.* (1995) *Brit. J. Dermatol.* 132, 745-749 which discusses soluble E-cadherin, page 4, line 1 of the specification.

It is clear from these references that sE-cadherin is a term which was well known in the art at the time of the priority date to refer to an 80kDa fragment of E-cadherin, and consequently it is sufficiently clear for the skilled person to understand what is meant by the references to it in the present patent claims.

In order to further clarify this term, the reference to "soluble E-cadherin" has been amended to "sE-cadherin" – the art-recognized designation of this fragment, in all claims. The basis for this amendment can be found on page 3, line 27.

In response to the examiners objections to the phrase "a method of treating a patient" in claim 5. The claimed method incorporates an evaluation phase and an administration of a therapeutic compound phase. Both of these are vital aspects of this method of treatment, as the diagnosis of the extent of the disease impacts on the choice of therapeutic intervention. Furthermore, as explained in the paragraph bridging pages 1-2 of the patent specification as published, COPD can be difficult to distinguish from other respiratory diseases by symptoms alone. The choice of treatment is dependent upon correct diagnosis and so evaluation and administration are integral parts of the method of treatment, as provided by the present invention.

In response to the examiners objections to the phrase "administering a compound" in Claim 5, line 4, the applicant is referring to any compound which is useful for treating the symptoms of COPD. Examples of compounds which treat COPD are well known in the art, some examples are given on page 1, lines 13-20 of the specification as filed: "Currently a number of pharmaceutical substances are indicated for or have been shown to be useful in treating the symptoms of COPD, including salmeterol xinafoate, fluticasone propionate and ipratropium bromide. (2R,3R,4S,5R)-2-[6-Amino-2-(1S-hydroxymethyl-2-phenyl-ethylamino)-purin-9-yl]-5-(2-ethyl-2H-tetrazol-5-yl)-tetrahydro-furan-3,4-diol is also of development interest in the treatment of COPD, as are tiotropium, 4-hydroxy-7-[2-[[2-[[3-(2-phenylethyoxy)propyl] sulfonyl]ethyl]amino]ethyl-2(3H)-benzothiazolone and cis-4-cyano-4-[3-(cyclopentyloxy)-4-methoxyphenyl]cyclohexanecarboxylic acid."

As the examiner himself admits on page 5 of the Official Action "it only involves routine practice in the art" to identify a compound to ameliorate the symptoms of COPD. Therefore it would be clear to a man skilled in the art which compound would be suitable to administer, once the extent of the disease had been evaluated.

In response to the examiner's objections to the phrase in Claim 5, line 4, "ameliorate the symptoms of the disease" - this does not refer to a single specific symptom of COPD, but to one or more symptoms of the disease. Page 1, lines 6-11, and page 2, lines 4-9 of the specification disclose symptoms of COPD, any or all of which the claimed method of treatment seeks to ameliorate.

The Applicant respectfully submits that in view of the forgoing remarks, the Applicant has overcome the Examiner's rejection under 35 U.S.C. §112, second paragraph, and the rejection should be withdrawn.

REJECTIONS UNDER 35 U.S.C. §103(a)

Claims 5-8, and 19-22 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Bullock, *et al.* (*J Allergy and Clinical Immunology (1998)* 101: S111)(hereinafter referred to as "Bullock") in view of a combination of Katayama, et al. (*International J. Oncology (1994)* 5: 1049-1057; Abstract)(hereinafter referred to as "Katayama") and Cioffi, *et al.* (*Tumori (1999)* 85: 32-34)(hereinafter referred to as "Cioffi").

Applicant respectfully traverses. *Bullock* provides a general disclosure, which was aimed at investigating whether alterations in levels of expression of E-cadherin, and α, β, and γ-catenins could be observed in different disease states including asthma, COPD, fibrosis, sarcoidosis and controls and whether there was any correlation between expression of these proteins and epithelial shedding and regeneration. There is no motivation from this abstract to pick sE-cadherin or any of the other proteins mentioned and to investigate any one of the diseases specified, as there is no indication that any one of the proteins is a better marker than any other protein for any one of the diseases. In addition, there is no teaching to select sE-cadherin and nothing to indicate to the skilled person that there might be a particular relationship between sE-cadherin and COPD, from amongst the list of disease states studied by *Bullock*.

Furthermore it is clear from this disclosure that *Bullock* failed to find a link between any of the different diseases (e.g. asthma and COPD) and the detectable amounts of the proteins under study, nor between the extent or progression of COPD and the amount of protein marker detected. In fact, *Bullock* expressly state that "Regardless of the disease status of the subject, areas of shedding or of regeneration were **always** associated with increased expression of both E-cadherin and α, β and γ-catenins." (emphasis added)

Katayama and Cioff disclose E-cadherin as a tumour marker, not as suggested by the examiner, as a lung dysfunction marker. There is no reason to assume that this protein would act the same way in a patient with COPD as it would in a patient with cancer. Katayama indicates that the E-cadherin levels are associated with cancer metastasis, a symptom that is unique to cancer and not an unrelated disease, such as COPD, which has a very different etiology.

Whilst it was known (see e.g. page 3, lines 25-29 of the specification as published) that sE-cadherin is found in the serum and methods for its detection were available, there is no suggestion in the cited documents of using FEV1 to correlate with the levels of sE-cadherin in the diagnosis and or prognosis of COPD. As stated above, there are several symptoms associated with COPD. There is no guidance in the prior art that FEV1 would be particularly useful for this type of correlation, in fact there is no suggestion to correlate any symptoms of COPD with sE-cadherin levels.

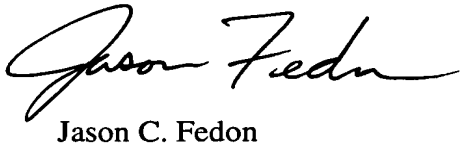
The present invention has made a novel link between FEV1 - a characteristic symptom of COPD - and sE-cadherin levels, has demonstrated that the marker varies predictably with disease severity *i.e.,* with changes in FEV1 and has demonstrated that this marker distinguishes COPD from other lung diseases such as asthma. None of this can be derived from *Bullock*, alone or in combination with *Katayama* or *Cioff*.

In view of the foregoing remarks, the Applicant respectfully requests that the Examiner withdraw the rejection of Claims 5-8, and 19-22 under 35 U.S.C. § 103(a).

The Applicant reserves the right to prosecute, in one or more patent applications, the claims to non-elected inventions, the claims as originally filed, and any other claims supported by the specification. The Applicant thanks the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration and allowance of the pending claims is earnestly solicited.

If it would expedite the prosecution of this application, the Examiner is invited to confer with the Applicant's undersigned agent.

Respectfully submitted,



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